REMARKS

Claims 1-9 are all the claims pending in the application. Applicants have amended the specification and claims 1-3 and 5-9 to rewrite the microorganism names in italics and to correct the spelling of "asymmetric".

Entry of the above amendments is respectfully requested.

Initially, Applicants thank the Examiner for acknowledging Applicants' claim to priority under 35 U.S.C. §119, and for confirming receipt of the priority document.

I. Objection to Specification

On page 2 of the Office Action, the Examiner objects to the disclosure because the microorganism names are not italicized and "asymmetric" is misspelled throughout the specification.

Applicants have amended the specification accordingly. Therefore, Applicants respectfully request that the objection be withdrawn.

II. Response to rejection of claims 7 under 35 U.S.C. § 112, first paragraph

On pages 2-3, the Examiner rejects claim 7 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants respectfully submit that the strains were present in the public domain. Accordingly, Applicants submit herewith catalogs (*Japan Collection of Microorganisms* and *List of Cultures*) that offered them for sale to the public. Applicants submit that since the microorganisms were available, the requirements of 35 U.S.C. §112 have been satisfied.

Therefore, Applicants respectfully request that the rejection be withdrawn.

III. **Response to rejection of claims 1-9 under 35 U.S.C. § 112, second paragraph**

On pages 3-4 of the Office Action, the Examiner rejects claims 1-9 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Initially, Applicants have amended the claims so that the names of the microbes are italicized, and have amended claims 1 and 8 to correct the spelling of "asymmetric". In addition, the parenthesis in the claims have been deleted and claim 5 has been amended to correct the spelling of "*Nocardia*".

With respect to the claim 1, Applicants submit that the phrase "ability being not inhibited seriously" is definite. The specification discloses that the phrase means that the converting ability in the presence of an inhibitor is about 70% or more of that in the absence of the inhibitor when assuming the ability in the absence of the inhibitor to be 100%". *See* page 5, lines 18-22. Accordingly, a person of skill in the art would understand the meaning of the phrase "ability being not inhibited seriously", and therefore would understand the scope of the claim.

With respect to claims 2 and 9, Applicants respectfully submit that the claims do further limit claims 1 and 8, respectively. Claims 2 and 9 further define which form optical isomer I and II are, and therefore limits claims 1 and 8 with respect to the process that is taken, i.e., a L-form is obtained from the D-form, whereas claim 1 is directed to a method where a L-form is obtained from the D-form or the D-form is obtained from the L-form.

With respect to claim 3, Applicants submit that the biological material is added to a mixture of D and L isomers, and have amended claim 3 accordingly. With respect to claim 4, Applicants submit that "whole" means "entire" cell (i.e., that the cell is intact (unbroken)". With respect to claims 5-7, Applicants have deleted "derived" and substituted therefor --obtained-- based on the Examiner's suggestion.

In view of the above, Applicants respectfully request that the rejections be withdrawn.

IV. Response to rejection of claims 1, 2, 5, 8 and 9 under 35 U.S.C. § 102(b)

On pages 4-5 of the Office Action, the Examiner rejects claims 1, 2, 5, 8 and 9 under 35 U.S.C. 102(b) as allegedly being anticipated by Wolfe et al. (U.S. Patent 4,510,246) or Laiz et al.

The Examiner cites Wolfe et al. as disclosing the use of epimerase obtained from *Streptomyces clavuligerus, cattleya* or *lipmanii* to epimerize isopenicillin N to penicillin N. *See* col. 4, lines 1-10. In addition, the Examiner cites Laiz et al. as disclosing an epimerase obtained from Nocardia *lactamdurans* or *Streptomyces clavuligerus* and its use to epimerize isopenicillin N.

Applicants respectfully traverse this rejection for the following reasons.

The present invention relates to a process for producing an optically active α-amino acid of formula (1), which comprises reacting an enantiomer of an optically active α-amino acid to be produced with a biological material, which has an ability of converting the enantiomer to the optically active α-amino acid, where the ability is not inhibited seriously by an amino acid transferase inhibitor β-chloro-D-alanine, β-chloro-L-alanine or gabaculine.

According to the present invention, an optically active amino acid is converted to its enantiomer rather than to a racemic mixture. Examples of the conversion of D-form amino acids to L-form thereof are clearly shown in Table 2, page 21 of the specification and a further example of the conversion of a racemic amino acid mixture to L-form thereof are shown in Table 3, page 21.

In contrast, Wolfe et al. and Laiz et al. do not teach or suggest converting an optical isomer of formula (1) of the present invention by converting it to its enantiomer.

Wolfe et al. refers to *S. clavuligerus*, particularly NRRL 3685 at col. 5, lines 59-63, which was harvested in Example 1 (at the bottom of col. 6) and used in the purification of isopenicillin N epimerase in Example 2 bridging from the bottom of col. 7 to col. 8. In Example 7, at lines 39 to 48, "SPCFX, an enzyme fraction, converted glycyl and N-acetyl compounds to penicillin and isopenicillin N", which is a mixture of optical isomers. In addition, from the last 2 lines of column 10 and the disclosure following, it is merely speculated that "substrate modified in the valinyl moiety *may be* cyclized" and "following epimerization of isopenicillin N analog to penicillin N analog". Further, Wolfe et al. describes that a cyclization mixture is a mixture of isopenicillin N and penicillin N. *See* col. 13, lines 26-30. As for *Nocardia lactamdurans*, Wolfe et al. does not provide any specific disclosure of its enzymatic activity.

Laiz et al. refers to isopenicillin epimerase derived from *S. clavuligerus*, NRRL 3585 on page 664. Laiz et al. discloses that the epimerase reaction is reversible. *See* left column of page 668. Laiz et al. also discloses that the reverse reaction was observed using pure preparations of penicillin N as substrate. Therefore, Laiz et al.

deals with the same enzyme as disclosed by Wolfe et al. above, and does not disclose more than Wolfe et al.

Although Wolfe et al. and Laiz et al. disclose epimerase, which can produce a racemic mixture of optical isomers based on the asymmetric carbon atom, neither reference discloses a method of producing one optical isomer of formula (1) by converting its enantiomer, as required in the present invention.

Accordingly, neither Wolfe et al. nor Laiz et al. teaches or suggests the present invention. Therefore, Applicants respectfully requests that the rejection be withdrawn.

V. **Response to rejection of claims 1-4, 8 and 9 under 35 U.S.C. § 102(e)**

On page 5 of the Office Action, the Examiner rejects claims 1-4, 8 and 9 under 35 U.S.C. 102(e) as allegedly being anticipated by Dicosimo et al. (U.S. 6,204,050).

The Examiner cites Dicosimo et al. as disclosing the use of 4-hydroxyproline epimerase obtained from A. *Baumanni* or S. *marcescens*, which may be used as whole cells, cell extracts or purified enzymes (*see* col. 2, l. 40) to contact at least one of trans-4-hydroxy-D-proline and cis-4-hydroxy-L-proline (col. 2, l. 55).

Applicants respectfully traverse this rejection for the following reasons.

Dicosimo discloses that trans-4-hydroxy-L-proline or cis-4-hydroxy-D-proline is converted to a mixture of cis-4-hydroxy-D-proline and trans-4-hydroxy-L-proline. *See* col. 3, lines 36-55. Therefore, Dicosimo is directed to epimerization to obtain a mixture. In addition, the structure of the hydroxyproline, which is a cyclic imine, is outside the scope of the α-amino acid of the present process.

Accordingly, although Dicosimo may disclose epimerase, Dicosimo does not teach or suggest converting one optical isomer of formula (1) to its enantiomer, as

required in the present invention. Therefore, Applicants respectfully submit that Dicosimo fails to teach the present invention, and respectfully request that the rejection be withdrawn.

VI. Response to rejection of claims 1-3, 5, 8 and 9 under 35 U.S.C. § 102/103

On page 5 of the Office Action, the Examiner rejects claims 1-3, 5, 8 and 9 under 35 U.S.C. 102(b) as allegedly being anticipated by, or obvious under 35 U.S.C. 103, over Lim et al. in light of the teachings of ATCC Catalog of Bacteria.

The Examiner cites Lim et al. as disclosing a racemase isolated from *Pseudomonas putida* that acts on the substrates of Table 3 as well as both L and D-threonine. Since microbes from the genus "*Flavimonas*" have been classified in the past by those of skill in the art as *Pseudomonas*, page 168 ATCC Catalog of Bacteria, the Examiner asserts that the use of microbes from genus *Flavimonas* is considered to be the same or obvious over the use of microbes from the genus *Pseudomonas*.

Applicants respectfully traverse this rejection for the following reasons.

Lim et al. discloses an epimerization reaction as disclosed in the abstract and that the enzyme reaction showed epimerization from L- to D-allo-threonine and also from D- to L-allo-threonine. In particular, Lim et al. discloses, in a section titled "Confirmation of threonine epimerization by ^{1}H-NMR" of the section that epimerization of L-threonine diminished the integration value of the α-proton signal of L-threonine to one half of the total integration value of the β proton signals of L-threonine and D-allo-threonine produced by epimerization. *See* right column, lines 9-12 on page 4214. This means that the epimerized product is a mixture of an equal amount of L-threonine and D-allo-threonine. Therefore, Lim et al. does not teach or suggest the claimed process

in which a completely different enzyme is used.

In addition, although some *Pseudomonas* microbes are correlated with some *Flavimonas* microbes due to the change of classification, there is no specific disclosure as to their ability in the ATCC catalog. Accordingly, it would not have been obvious for a person of ordinary skill in the art to arrive at the present invention in view of Lim in light of ATCC catalog.

In particular, it appears as though the Examiner is using hindsight to pick and chose the particular microbes of the present invention from the various microbes, which is improper. The teaching or suggestion to make the claimed combination must be found in the prior art, not in applicant's disclosure. *See* MPEP 2143 (citing *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)).

In view of the above, Applicants respectfully submit that Liam et al. does not teach or suggest the present invention, and respectfully request that the rejection be withdrawn.

VII. Response to rejection of claims 1-3, 8 and 9 under 35 U.S.C. § 103

On page 6 of the Office Action, the Examiner rejects claims 1-3, 8 and 9 under 35 U.S.C. 103(a) as allegedly being unpatentable over Gosling et al. or Hashimoto et al.

The Examiner cites Gosling et al. as disclosing that a microbe from *Rhizobium* possesses an alanine racemase. In addition, the Examiner cites Hashimoto et al. as deducing that a microbe from *Arthrobacter* has D-alanine racemase activity. Although the above references do not specifically demonstrate or isolate the racemase activity from the above genera, the Examiner asserts that the named activity strongly suggests to one of skill in the art to catalyze the racemization of alanine from either D or L

alanine or a non-racemic mixture of the two isomers.

Therefore, the Examiner takes the position that one of ordinary skill in the art would have been motivated to make these substitutions in order to obtain the resulting compound, as suggested by the references, with a reasonable expectation of success.

Applicants respectfully traverse this rejection for the following reasons.

Hashimoto et al. discloses that L-alanine was converted to D-alanine where D-alanine formation proceeded until almost half of the L-alanine had disappeared, at which time the amount of D-alanine formed was roughly equivalent to the L-alanine lost. *See* right column, second paragraph on page 386. This means that a racemic mixture was formed. Therefore, Hashimoto et al. does not teach or suggest the presently claimed process, which converts an optical isomer into its enantiomer.

Gosling et al. merely refers to D-amino-acid aminotransferase and alanine racemase but no specific disclosure thereof is made.

Neither Hashimoto et al. nor Gosling et al. disclose the activity as claimed in claim 1 to convert one optical isomer of formula (1) to its enantiomer. Therefore, Hashimoto et al. and Gosling et al. do not teach or suggest the present invention, which is not directed to racemization.

Accordingly, Applicants respectfully request that the rejection be withdrawn..

VIII. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone

interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicant hereby petitions for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification is changed as follows:

Page 2, the second paragraph:

Now we discovered a biological material which has an ability of converting one of the optical isomers of a certain amino acid to the other of the optical isomers, the isomerism being on the basis of an [assymetric] asymmetric carbon atom to which both of an amino group and a carboxyl group are bound and the ability described above being not inhibited seriously by an amino acid transferase inhibitor β-chloro-D-alanine, β-chloro-L-alanine or gabaculine, and finally established the present invention by applying said biological material to the production of an optically active amino acid of the amino acid described above.

Page 2, the paragraph bridging pages 2 and 3:

1. a method for producing from one of the optical isomers (optical isomer I) of an amino acid represented by Formula (1):

$$R\text{-}CH(NH_2)\text{-}COOH \quad (1)$$

(wherein R is an optionally substituted C1-C12 alkyl group, an optionally substituted C4-C8 cycloalkyl group or an optionally substituted C6-C14 aryl group) (hereinafter, it is sometimes referred to as the amino acid (1)) the other of the optical isomers (optical isomer II), said method comprising reacting a biological material which has an ability of converting said one of the optical isomers (optical isomer I) to said the other of the optical isomers (optical isomer II), the isomerism being on the basis of an [assymetric]

asymmetric carbon atom to which both of an amino group and a carboxyl group are bound and said ability being not inhibited seriously by an amino acid transferase inhibitor β-chloro-D-alanine, β-chloro-L-alanine or gabaculine, with said one of the optical isomers (optical isomer I). (Hereinafter, it is sometimes referred to as the method of the present invention.)

Page 3, the fourth and fifth paragraphs:

5. the method according to the above 1, wherein said biological material is one derived from a microorganism belonging to the genus [Arthrobacter, Flavimonas, Klebsiella, Norcadia, Pseudomonas, Rhizobium, Saccharopolyspora or Streptomyces] *Arthrobacter, Flavimonas, Klebsiella, Nocardia, Pseudomonas, Rhizobium, Saccharopolyspora* or *Streptomyces*.

6. the method according to the above 1, wherein said biological material is one derived from a microorganism classified to [Arthrobacter pascens, Flavimonas oryzihabitans, Klebsiella planticola, Nocardia diaphanozonaria, Pseudomonas chlororaphis, Pseudomonas oleovorans, Pseudomonas oxalaticus, Pseudomonas taetrolens, Rhizobium meliloti, Saccharopolyspora hirsuta or Streptomyces roseus] *Arthrobacter pascens, Flavimonas oryzihabitans, Klebsiella planticola, Nocardia diaphanozonaria, Pseudomonas chlororaphis, Pseudomonas oleovorans, Pseudomonas oxalaticus, Pseudomonas taetrolens, Rhizobium meliloti, Saccharopolyspora hirsuta* or *Streptomyces roseus*.

Page 5, the paragraph bridging pages 5 and 6:

7. the method according to the above 1, wherein said biological material is one derived from [Arthrobacter pascens strain IFO12139, Flavimonas oryzihabitans strain

JCM2952, Klebsiella planticola strain JCM7251, Nocardia diaphanozonaria strain JCM3208, Pseudomonas chlororaphis strain IFO3521, Pseudomonas oleovorans strain IFO13583, Pseudomonas oxalaticus strain IFO13593, Pseudomonas taetrolens strain IFO3460, Rhizobium meliloti strain IFO14782, Saccharopolyspora hirsuta subsp.kobensis strain JCM9109 or Streptomyces roseus] *Arthrobacter pascens* strain IFO12139, *Flavimonas oryzihabitans* strain JCM2952, *Klebsiella planticola* strain JCM7251, *Nocardia diaphanozonaria* strain JCM3208, *Pseudomonas chlororaphis* strain IFO3521, *Pseudomonas oleovorans* strain IFO13583, *Pseudomonas oxalaticus* strain IFO13593, *Pseudomonas taetrolens* strain IFO3460, *Rhizobium meliloti* strain IFO14782, *Saccharopolyspora hirsuta subsp.kobensis* strain JCM9109 or *Streptomyces roseus* strain IFO12818.

Page 4, the first full paragraph:

8. a method for improving the optical purity of an amino acid represented by Formula (1):

$$R\text{-}CH(NH_2)\text{-}COON \qquad (1)$$

(wherein R is an optionally substituted C1-C12 alkyl group, an optionally substituted C4-C8 cycloalkyl group or an optionally substituted C6-C14 aryl group), said method comprising reacting a biological material which has an ability of converting one of the optical isomers (optical isomer I) of said amino acid to the other of the optical isomers (optical isomer II), the isomerism being on the basis of an [assymetric] asymmetric carbon atom to which both of an amino group and a carboxyl group are bound and said ability being not inhibited seriously by an amino acid transferase inhibitor β-chloro-D-alanine, β-chloro-L-alanine or gabaculine, with said amino acid represented by

Formula (1).

Page 5, the fourth paragraph:

A biological material which can be employed in the present invention is a biological material which has an ability of converting one of the optical isomers (optical isomer I) of the amino acid (1) to the other of the optical isomers (optical isomer II), the isomerism being on the basis of an [assymetric] asymmetric carbon atom to which both of an amino group and a carboxyl group are bound and the ability being not inhibited seriously by an amino acid transferase inhibitor β-chloro-D-alanine, β-chloro-L-alanine or gabaculine (hereinafter sometimes referred to as the biological material of the present invention.

Page 7, the paragraph bridging pages 7 and 8:

A preferred example of the biological material of the present invention may be a material derived from a microorganism belonging to the genus [Arthrobacter, Flavimonas, Klebsiella, Norcadia, Pseudomonas, Rhizobium, Saccharopolyspora and Streptomyces, preferably a material derived from a microorganism classified to Arthrobacter pascens, Flavimonas oryzihabitans, Klebsiella planticola, Nocardia diaphanozonaria, Pseudomonas chlororaphis, Pseudomonas oleovorans, Pseudomonas oxalaticus, Pseudomonas taetrolens, Rhizobium meliloti, Saccharopolyspora hirsuta and Streptomyces roseus, and typically a material derived from Arthrobacter pascens strain IFO12139, Flavimonas oryzihabitans strain JCM2952, Klebsiella planticola strain JCM7251, Nocardia diaphanozonaria strain JCM3208, Pseudomonas chlororaphis strain IFO3521, Pseudomonas oleovorans strain IFO13583, Pseudomonas oxalaticus strain IFO13593, Pseudomonas taetrolens strain IFO3460, Rhizobium meliloti strain

IFO14782, Saccharopolyspora hirsuta subsp.kobensis strain JCM9109 and Streptomyces roseus] *Arthrobacter, Flavimonas, Klebsiella, Nocardia, Pseudomonas, Rhizobium, Saccharopolyspora* and *Streptomyces*, preferably a material derived from a microorganism classified to *Arthrobacter pascens, Flavimonas oryzihabitans, Klebsiella planticola, Nocardia diaphanozonaria, Pseudomonas chlororaphis, Pseudomonas oleovorans, Pseudomonas oxalaticus, Pseudomonas taetrolens, Rhizobium meliloti, Saccharopolyspora hirsuta* and *Streptomyces roseus*, and typically a material derived from *Arthrobacter pascens* strain IFO12139, *Flavimonas oryzihabitans* strain JCM2952, *Klebsiella planticola* strain JCM7251, *Nocardia diaphanozonaria* strain JCM3208, *Pseudomonas chlororaphis* strain IFO3521, *Pseudomonas oleovorans* strain IFO13583, *Pseudomonas oxalaticus* strain IFO13593, *Pseudomonas taetrolens* strain IFO3460, *Rhizobium meliloti* strain IFO14782, *Saccharopolyspora hirsuta subsp.kobensis* strain JCM9109 and *Streptomyces roseus* strain IFO12818.

Page 16, the paragraph bridging pages 16 and 17:

A 500 mL Sakaguchi flask containing 100 ml of a sterilized medium (pH 7.0) containing 1.0 % (w/v) glycerol, 0.2 % (w/v) polypeptone (Nihon Pharmaceutical Co., Ltd.), 0.3 % (w/v) meat extract powder (Kyokuto Pharmaceutical Ind., Co., Ltd.), 0.3 % (w/v) yeast extract (Difco), 0.1 % (w/v) dipotassium phosphate, 0.1 % (w/v) mono potassium phosphate, 0.03 % (w/v) magnesium sulfate heptahydrate was inoculated with 1 mL of a culture of [Nocardia diaphanozonaria] *Nocardia diaphanozonaria* strain JCM3208 which had previously been cultivated in a medium of the similar composition, and incubated at 30°C for 3 days with a reciprocal shaking. From this culture, cells were collected by centrifugation (10000 g, 10 minutes), which was

combined with 10 ml of 100mM potassium phosphate buffer (pH 7.0) to form a cell suspension again, which was centrifuged (10000 g, 10 minutes) to obtain wet cells. The wet cells thus obtained were suspended in 10 mL of 100mM potassium phosphate buffer (pH 7.0) to obtain a cell suspension. 50 mg of D-p-chlorophenylalanine was dissolved in 45 mL of an aqueous solution (pH 7.0) containing 0.15 % (w/v) mono potassium dihydrogen phosphate, 0.15 % (w/v) disodium hydrogen mono phosphate, 0.02 % (w/v) magnesium sulfate heptahydrate, 0.001 % (w/v) ferrous sulfate heptahydrate, 0.001 % (w/v) zinc sulfate heptahydrate, 0.001 % (w/v) manganese sulfate trihydrate, 0.001 % cobalt chloride hexahydrate and 0.0005 % (w/v) yeast extract, to which 5 ml of the cell suspension described above was added and the reaction mixture was kept at 30°C for 74 hours with stirring using a magnetic stirrer at 1000 rpm. Subsequently, an aliquot of the reaction mixture was taken and centrifuged to remove the cell and the supernatant obtained was subjected to HPLC to ensure that L-p-chlorophenylalanine at the optical purity of 100 % e.e. was obtained at 79 yield.

Page 20, Table 1:

Biological material	Incubation time (h)	% L-form	% D-form
[Arthrobacter pascens] *Arthrobacter pascens* strain IFO12139	72	64	36
[Flavimonas oryzihabitans] *Flavimonas oryzihabitans* strain JCM2952	72	90	10
[Klebsiella planticola] *Klebsiella planticola* strain JCM7251	48	61	39
[Pseudomonas chlororaphis] *Pseudomonas chlororaphis* strain IFO3521	72	94	6
[Pseudomonas oleovorans] *Pseudomonas oleovorans* strain IFO13583	48	89	11
[Pseudomonas oxalaticus] *Pseudomonas oxalaticus* strain IFO13593	48	75	25

[Pseudomonas taetrolens] *Pseudomonas taetrolens* strain IFO3460	72	90	10
[Rhizobium meliloti] *Rhizobium meliloti* strain IFO14782	48	84	16
[Saccharopolyspora hirsuta subsp.kobensis] *Saccharopolyspora hirsuta subsp.kobensis* strain JCM9109	72	67	33
[Streptomyces roseus] *Streptomyces roseus* strain IFO12818	48	96	4

Page 20, Table 2:

Biological material	Incubation time (h)	% L-form	% D-form
[Arthrobacter pascens] *Arthrobacter pascens* strain IFO12139	72	100	0
[Flavimonas oryzihabitans] *Flavimonas oryzihabitans* strain JCM2952	72	100	0
[Klebsiella planticola] *Klebsiella planticola* strain JCM7251	48	100	0
[Pseudomonas chlororaphis] *Pseudomonas chlororaphis* strain IFO3521	72	100	0
[Pseudomonas oleovorans] *Pseudomonas oleovorans* strain IFO13583	48	100	0
[Pseudomonas oxalaticus] *Pseudomonas oxalaticus* strain IFO13593	48	100	0
[Pseudomonas taetrolens] *Pseudomonas taetrolens* strain IFO3460	72	100	0
[Rhizobium meliloti] *Rhizobium meliloti* strain IFO14782	48	100	0
[Saccharopolyspora hirsuta subsp.kobensis] *Saccharopolyspora hirsuta subsp.kobensis* strain JCM9109	72	100	0
[Streptomyces roseus] *Streptomyces roseus* strain IFO12818	48	100	0

Page 22, the paragraph bridging pages 22 and 23:

A 500 mL Sakaguchi flask containing 100 ml of a sterilized medium (pH 7.0) containing 1.0 % (w/v) glycerol, 0.2 % (w/v) polypeptone (Nihon Pharmaceutical

Co., Ltd.), 0.3 % (w/v) meat extract (Kyokuto Pharmaceutical Ind., Co., Ltd.), 0.3 % (w/v) yeast extract (Difco), 0.1 % (w/v) dipotassium phosphate, 0.1 % (w/v) potassium mono phosphate, 0.03 % (w/v) magnesium sulfate heptahydrate was inoculated with 1 mL of a culture of [Nocardia diaphanozonaria] *Nocardia diaphanozonaria* strain JCM3208 which had previously been cultivated in a medium of the similar composition, and incubated at 30°C for 2 days with a reciprocal shaking. 80 ml of this culture was subjected to centrifugation (10000 g, 10 minutes) to collect wet cells. The collected wet cells were washed twice with 80 ml of 100mM potassium phosphate buffer (pH 7.0) and the wet cells thus obtained was suspended in 4 mL of 100mM potassium phosphate buffer (pH 7.0) to obtain a cell suspension.

Page 24, the first paragraph:

The reaction was performed similarly as in Example 6 except for using each of the microorganisms shown in Table 7 instead of [Nocardia diaphanozonaria] *Nocardia diaphanozonaria* strain JCM3208. The results are shown in Table 7.

Page 24, Table 7:

Biological material	Relative value (%)			
	Absence	β-Chloro-D-alanine	β-Chloro-L-alanine	Gabaculine
[Flavimonas oryzihabitans] *Flavimonas oryzihabitans* JCM2952	100	144	92	105
[Klebsiella planticola] *Klebsiella planticola* JCM7251	100	90	92	102
[Pseudomonas chlororaphis] *Pseudomonas chlororaphis* IFO3521	100	85	102	72
[Pseudomonas oleovorans] *Pseudomonas oleovorans* IFO13583	100	91	94	87
[Pseudomonas taetrolens] *Pseudomonas taetrolens* IFO3460	100	84	87	75
[Rhizobium meliloti] *Rhizobium meliloti* IFO14782	100	108	96	88

Page 24, the second paragraph:

The reaction was performed similarly as in Example 6 except for using each of the microorganisms shown in Table 8 instead of [Nocardia diaphanozonaria] *Nocardia diaphanozonaria* strain JCM3208 and except that the reaction time was 24 hours (when the reaction was equilibrated). The results are shown in Table 8.

Page 24, Table 8:

Biological material	Relative value (%)			
	Absence	P-Chloro-D-alanine	P-Chloro-L-alanine	Gabaculine
[Arthrobacter pascens] *Arthrobacter pascens* IFO12139	100	83	84	96
[Pseudomonas oxalaticus] *Pseudomonas oxalaticus* IFO13593	100	124	91	105
[Saccharopolyspora hirsuta] *Saccharopolyspora hirsuta* JCM9109	100	99	101	97
[Streptomyces roseus] *Streptomyces roseus* IFO12818	100	114	95	97

IN THE CLAIMS:

The claims have been amended as follows.

1. (Amended) A method for producing from an [one of the optical isomers (]optical isomer I[)] of an amino acid represented by Formula (I):

$$R\text{-}CH(NH_2)\text{-}COOH \qquad (1)$$

[(wherein] wherein R is an optionally substituted C1-C12 alkyl group, an optionally substituted C4-C8 cycloalkyl group or an optionally substituted C6-C14 aryl [group)] group, [the other of the optical isomers (] an optical isomer II[)], said method comprising reacting a biological material which has an ability of converting said [one

of the optical isomers (]optical isomer I[)] to said [the other of the optical isomers (]optical isomer II[)], the isomerism being on the basis of an [assymetric] asymmetric carbon atom to which both of an amino group and a carboxyl group are bound and said ability being not inhibited seriously by an amino acid transferase inhibitor β-chloro-D-alanine, β-chloro-L-alanine or gabaculine, with said [one optical isomers (]optical isomer I[)].

2. (Amended) The method according to Claim 1, wherein said [one of the optical isomers (]optical isomer I[)] is a D-form and said [the other of the optical isomers (]optical isomer II[)] is a L-form.

3. (Amended) The method according to Claim 1, wherein said [one of the optical isomers (]optical isomer I[)] with which said biological material is reacted is present in a mixture with [of said the other of the optical isomers (]optical isomer II[)].

5. (Amended) The method according to Claim 1, wherein said biological material is one [derived] obtained from a microorganism belonging to the genus [Arthrobacter, Flavimonas, Klebsiella, Norcadia, Pseudomonas, Rhizobium, Saccharopolyspora or Streptomyces] *Arthrobacter, Flavimonas, Klebsiella, Nocardia, Pseudomonas, Rhizobium, Saccharopolyspora* or *Streptomyces*.

6. (Amended) The method according to Claim 1, wherein said biological material is one [derived] obtained from a microorganism classified to [Arthrobacter pascens, Flavimonas oryzihabitans, Klebsiella planticola, Nocardia diaphanozonaria, Pseudomonas chlororaphis, Pseudomonas oleovorans, Pseudomonas oxalaticus, Pseudomonas taetrolens, Rhizobium meliloti, Saccharopolyspora hirsuta or Streptomyces roseus] *Arthrobacter pascens, Flavimonas oryzihabitans, Klebsiella*

planticola, *Nocardia diaphanozonaria*, *Pseudomonas chlororaphis*, *Pseudomonas oleovorans*, *Pseudomonas oxalaticus*, *Pseudomonas taetrolens*, *Rhizobium meliloti*, *Saccharopolyspora hirsuta* or *Streptomyces roseus*.

7. (Amended) The method according to Claim 1, wherein said biological material is one [derived] obtained from [Arthrobacter pascens strain IFO12139, Flavimonas oryzihabitans strain JCM2952, Klebsiella planticola strain JCM7251, Nocardia diaphanozonaria strain JCM3208, Pseudomonas chlororaphis strain IFO3521, Pseudomonas oleovorans strain IFO13583, Pseudomonas oxalaticus strain IFO13593, Pseudomonas taetrolens strain IFO3460, Rhizobium meliloti strain IFO14782, Saccharopolyspora hirsuta subsp.kobensis strain JCM9109 or Streptomyces roseus strain IFO12818] *Arthrobacter pascens* strain IFO12139, *Flavimonas oryzihabitans* strain JCM2952, *Klebsiella planticola* strain JCM7251, *Nocardia diaphanozonaria* strain JCM3208, *Pseudomonas chlororaphis* strain IFO3521, *Pseudomonas oleovorans* strain IFO13583, *Pseudomonas oxalaticus* strain IFO13593, *Pseudomonas taetrolens* strain IFO3460, *Rhizobium meliloti* strain IFO14782, *Saccharopolyspora hirsuta subsp.kobensis* strain JCM9109 or *Streptomyces roseus* strain IFO12818.

8. (Amended) A method for improving the optical purity of an amino acid represented by Formula (I):

$$R\text{-}CH(NH_2)\text{-}COOH \qquad (1)$$

[(wherein] wherein R is an optionally substituted C1-C12 alkyl group, an optionally substituted C4-C8 cycloalkyl group or an optionally substituted C6-C14 aryl [group)] group, said method comprising reacting a biological material which has an ability of converting an [one of the optical isomers (]optical isomer I[)] of said amino

acid to an [the other of the optical isomers (]optical isomer II[)], the isomerism being on the basis of an [assymetric] asymmetric carbon atom to which both of an amino group and a carboxyl group are bound and said ability being not inhibited seriously by an amino acid transferase inhibitor β-chloro-D-alanine, β-chloro-L-alanine or gabaculine, with said amino acid represented by Formula (I).

9. (Amended) The method according to Claim 8, wherein said [one of the optical isomers (]optical isomer I[)] is a D-form and said [the other of the optical isomers (]optical isomer II[)] is a L-form.